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(54) Alkoxy carbonylation or carbonylation with CO and organic hydroxyl compound.

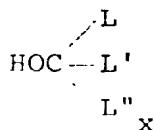
(57) The reaction of enol acylates with CO and organic hydroxyl compounds to produce esters hydrolyzable to hydroxy acids, is described. The enol acylate may be vinyl acetate and the hydroxy acid may be lactic acid.

**EP 0 144 118 A1**

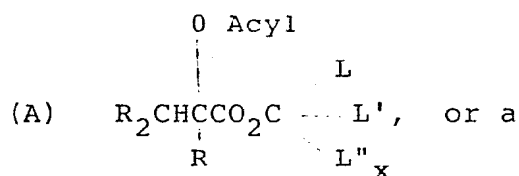
This invention relates to a new reaction wherein an enol acylate is reacted with CO and a hydroxyl compound to add an esterified carboxy group to the vinyl enol carbon atom of the enol acylate. The enol acylate may be vinyl acetate in a now preferred embodiment of the process, and the esterified product can be hydrolyzed to produce lactic acid.

More specifically, according to the present invention we provide a process comprising intimately admixing and reacting an enol acylate,  $R_2C=C-O-Acyl$ ,  
 $\quad \quad \quad |$   
 $\quad \quad \quad R$

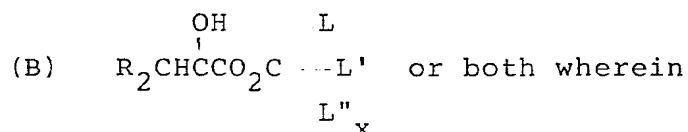
with CO and a hydroxyl compound



which is free of ethylenic or acetylenic unsaturation to produce an acyloxy ester compound,

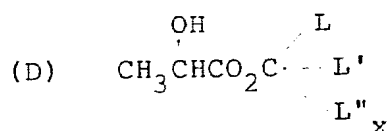
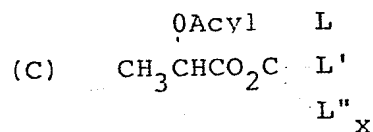


a hydroxy ester compound,



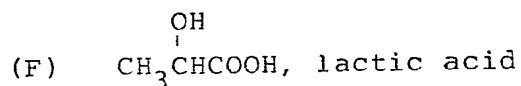
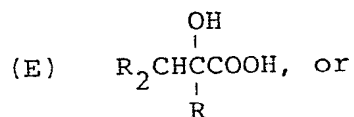
each R is H or  $C_1$  to  $C_{30}$  hydrocarbyl, usually H or  $C_1$  to  $C_{10}$  hydrocarbyl, and each R is the same or different, and L, L' and L'' are each H or an organic radical and L and L' can be members of a ring together with C, and x either is zero or 1 as necessary to satisfy the valence of the carbon atom, and wherein each of L, L', L'' and said Acyl radicals can contain up to 30, usually up to 10, carbon atoms. Most usually each R group is limited to a maximum of 10 carbon atoms, all of which are members of an open chain hydrocarbyl group.

In a more particular aspect of the invention the enol acylate reactant is a vinyl acylate,  $H_2C=CHOAcyl$ , (the foregoing enol acylate where all R's are H) and compounds (A) and (B) become respectively, compounds (C) and (D):



In all of the above L, L' and L" and the residue of the Acyl attached to the Acyl O atom are usually hydrocarbyl. Moreover, the enol acylate is always free of acetylenic unsaturation and contains only one ethylenic double bond.

In another aspect of the invention, there is provided a two step process in which the product (A) and/or (B) including (C) and/or (D) is hydrolyzed to the alpha hydroxy acid:



The process of the present invention when applied to a vinyl acylate reactant is of special importance since compounds (C) and (D) are precursors of lactic acid, compound (F), important commercially in the baking industry, in the cheese industry, in dyeing wool, in alkyd resins, to make plasticizers for resins, etc. It is particularly applicable when the vinyl acylate is vinyl acetate, since the latter raw material is inexpensive and readily available.

This embodiment of the invention, the last-mentioned

aspect, is especially important since lactic acid has heretofore been made by relatively disadvantageous processes.

Thus, lactic acid is currently produced either by fermentation, usually of molasses, or by a multistep non-catalytic route involving HCN hydrocyanation of acetaldehyde followed by hydrolysis of the product cyanohydrin with  $H_2SO_4$  to yield a stoichiometric amount of  $(NH_4)_2SO_4$  along with lactic acid. The fermentation process is costly and inefficient in that it produces large amounts of by-products, making product purification expensive and troublesome. The chemical route is highly corrosive, consumes stoichiometric amounts of toxic HCN and  $H_2SO_4$ , is expensive, based on HCN prices, and produces stoichiometric quantities of ammonium sulfate, a low-grade fertilizer difficult to sell at a profit.

It is an object of the present invention to provide a process for making compounds of the formula (A) or (B), precursors for 2-hydroxycarboxylic acids, including compounds of formulas (C) and (D), precursors for lactic acid, by an economically advantageous route.

It is another object of the invention to provide such a process for making lactic acid precursors, and for making lactic acid therefrom by hydrolysis, which avoids the disadvantages of the foregoing conventional processes.

Other objects, as well as aspects, features, and advantages of the present invention will become apparent from the description, examples and claims herein.

The foregoing objects are realized according to the process of the present inventions, which process utilizes inexpensive CO to replace HCN as the carbon source and is capable of producing the esters of compounds (A) and (B) in high yields at high conversions and selectivities. Furthermore, the present process results in essentially no non-recyclable or other undesirable by-products. Note that compounds (A), (B), (C) and (D) are hydrolyzable

to the 2-hydroxy carboxylic acid, lactic acid in the case of (C) and (D).

We believe that we are the first to discover or disclose the carbonylation or carboxylation reaction of an enol acylate with a CO and a hydroxyl compound such as an alcohol or the like.

Thus, in U.S. Patent 4,257,973 there is disclosed in column 2 the alkoxycarbonylation of certain acyloxy-olefinic compounds in which the acyloxy group is attached to a carbon atom which is part of a hydrocarbyl group which is in turn attached to a carbon atom of an ethylenic double bond. A similar structure is disclosed in U.S. Patent 3,859,319. However, neither patent discloses the reaction of the alkoxycarbonylation of an enol acylate with CO and a hydroxyl compound, although each prior art patent discloses this type of reaction with a very wide variety of aliphatically unsaturated compounds, using particular organophosphorus palladium halides as catalysts.

U.S. Patent 4,377,708 discloses the hydrocarboxylation of enol esters such as vinyl acetate and other vinyl esters using CO and water as reactants with the enol esters. Special precautions are taken to provide for stability of catalyst, product and starting material in the presence of the water reactant, and care must be taken to provide for the presence of only a small fraction of the water required for the reaction; thus usually the water is kept at a concentration of no more than about 3 weight percent of the reaction medium, so as to avoid hydrolysis of the ester starting material such as vinyl acetate to form an enol and a carboxylic acid, which enol can and will rearrange to an aldehyde.

The present process avoids the problem of hydrolysis with water. Furthermore, as will be seen, much higher yields can be produced in the present process; the best in U.S. 4,377,708 being 76 percent selectivity at 98 percent conversion, amounting to about 74.5 percent yield, well below the yield of products hydro-

lyzable to lactic acid that can be made in the present process.

German patent 1,221,224 discloses carboxylation with CO and alcohols or phenols. The substrates disclosed are olefinic compounds but do not include any enol acylates. Swiss patent 589,571 is similar and also does not disclose any enol acylate starting material.

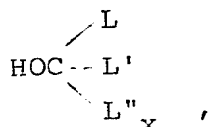
Enol acylates are potentially subject to the probability or possibility of instability in a reaction involving an alcohol or the like because some transesterification could take place to make an enol, which is unstable and would decompose to a saturated aldehyde. No such problem exists in the alkylcarboxylation of olefinic materials such as allyl acetate or methyl acrylate because no enols are potentially involved.

The hydrocarboxylation reaction is carried out catalytically, discussed in more detail hereafter. It can also be carried out continuously or in batch operation in the liquid or vapor phases. Usually the reaction is carried out in batchoperation in a solvent under pressure.

The reactant concentrations can vary widely and are not critical. The ratio of hydroxyl reactant to the enol ester is usually no greater than 10/1 on a molar basis. The amount of monoxide can vary widely, but it is preferred to carry out the reaction under a carbon monoxide pressure of 15 to 3500 psig, preferably 500 to 2500 psig. The amount of catalyst can also vary widely. Most conveniently, the amount of catalyst is between 0.01 and 100 mole percent based on the enol ester, more usually 0.1 to 10 mole percent.

Usually, the reactant is carried out with a solvent. The solvent should be inert under the reaction conditions and should dissolve the reactants and desirably dissolve the active catalyst species, although heterogenous catalysts are possible. Suitable solvents are tetrahydrofuran, benzene,  $\text{CH}_3\text{CN}$ , diethyl ether, diethylene glycol dimethyl ether,  $\text{CH}_2\text{Cl}_2$  and  $\text{CH}_3\text{Cl}$ . The now preferred solvent is tetrahydrofuran, particularly when using  $(\phi_3\text{P})_2\text{PdCl}_2$  or

Pd(P $\phi$ )<sub>4</sub> catalyst, or other palladium compounds, although an excess of the hydroxyl compound is also especially usefull. Usually, the amount of solvent in the system will be such that the enol ester concentration is at least about 0.01 weight percent in the solution. A special case of a solvent that is not inert, strictly speaking, under the reaction conditions is either of the starting material reactants, i.e., the enol ester or the hydroxy compound. Either can be used in excess of the stoichiometric amount to react with the other reactant. Use of a large excess of the compound



whether or not another solvent, such as THF, is present, helps produce appreciable amounts of compound (B); thus, the Acyl group is transesterified during the main carboxylation step.

The reaction is normally carried out at a temperature of 0 to 250°C, preferably 20 to 150°C. However, the reaction temperature can be below or above this if desired. As will be understood, optimum reaction temperature varies with the specific reactants. Reaction times on the order of 0.1 to 250 hours can be employed, with reaction times on the order of 2 to 50 hours being more convenient.

While a wide variety of complexes of transition metals are known as catalysts for the hydrocarboxylation of alkenes (See, for instance, 1) Pino, P., Piacenti, F., in Organic Synthesis via Metal Carbonyls, Volume 2, Wender, I., Pino, P., eds., Wiley, New York, 1977, pp. 233-296; 2) Falbe, J., New Syntheses with Carbon Monoxide, New York, Springer Verlag, Chapter 3 and 5; 3) Forster, D.,; Hershman, A.,; Morris, D.E., Catal. Rev. Sci. Eng. 23, 89-105 (1981); 4) Parshall, G.W., Catal. Rev. Sci.- Eng., 23, 107-124(1981); 5) Bittler, J.V. Kutepow, N., Neubauer, D., Reis, H., Angew. Chem. Intl. Ed. Eng., 7, 329-335 (1968),) no disclosures were found using such catalysts to react an

enol acylate with CO and an organic hydroxyl compound. Catalysts useful are generally transition metal compounds, particularly coordination complexes of such metals. We have discovered that palladium coordination complexes are  
 5 remarkably effective, and especially those complexed with a phosphine, such as  $P\phi_3$ , when considered in the light of experience with other known transition metal catalyst complexes for hydrocarboxylation of alkenes, or for hydro-  
 10 formylation for enol ethers or enol acetates (U.S. Patent 3,888,880; B.Fell, M.Barl, J.Mol.Catal., 1977, 2, 301-6; Tinker, Harold B. (Monsanto) Ger. Offen. 2,623,673; U.S. 4,072,709). Especially useful Pd complexes are  $(\phi_3P)_2PdCl_2$  and  $(\phi_3P)_4Pd$  with or without a promoter or "co-catalyst" such as HCl or  $P\phi_3$ .

15 Once a reaction is completed, the ester products can be recovered from the reaction system in a conventional manner, such as for example, by vacuum distillation.

Especially useful hydroxyl compounds in the reaction with the enol acylates and CO are hydroxyalkanes having  $C_1$   
 20 to  $C_4$  carbon atoms, and phenol.

The second step in the overall process of the invention is the hydrolysis of the esters (A) and/or (B) to the alpha-hydroxy acid, lactic acid in the special case of the ester products (C) and (D). This reaction is a conventional  
 25 hydrolysis reaction. It is catalyzed by any dilute aqueous acid or base. Suitable acids or bases are HCl,  $H_2SO_4$ ,  $HNO_3$ ,  $H_3PO_4$ , acetic acid, KOH, NaOH,  $NH_4OH$  or pyridine. The reaction is conveniently carried out at temperatures at above  $0^\circ C$  to  $120^\circ C$ , more usually about 20 to  $100^\circ C$ . If  
 30 desired, non-interfering hydrophilic solvents other than water can be employed. Examples of such solvents are tetrahydrofuran,  $CH_3CN$ , and the like. Reaction times on the order of 0.1 to 24 hours, usually 0.5 to 4 hours, can be employed.

35 An alternate method of carrying out the hydrolysis of compounds (A) or (B) is to treat (A) or (B) with  $H_2O$  in the gas phase (temperature  $100-250^\circ C$ ) with or without catalyst.

The 2-hydroxy acid product of the hydrolysis can be



recovered from the reaction medium in a conventional manner. For example, the reaction product can be recovered by precipitation as the calcium salt. Alternatively, low boiling by-product components of the hydrolysis product mixture can be removed by fractional distillation, and the remaining lactic acid or other 2-hydroxy acid solution in water can be sold as end product.

If the 2-hydroxy acid is produced by the gas phase reaction described above, it can be isolated in pure form from the reaction effluent by fractional distillation and stored either as pure compound or in aqueous solution.

It will be noted that, as understood in the art, aqueous solutions of lactic acid more concentrated than 20 percent will tend to polymerize.

The above reaction scheme comprising reactions (1) to (3) provides a simple and straightforward system for producing 2-hydroxy acids using an enol acylate starting material. As can be seen, it totally avoids the use of costly and deleterious HCN and the production of unwanted by-product ammonium sulfate, with the consumption of large amounts of sulfuric acid.

The following examples are merely illustrative and are not to be considered as limiting.

EXAMPLE 1

0.48 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Ten mole percent, based on vinyl acetate, of a catalyst comprising bis(triphenylphosphine)dichloropalladium,  $(\phi_3P)_2PdCl_2$ , was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system.

The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allow to react for 44 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that conversion was 84.5 percent and that methyl 2-acetyloxypropanoate was produced in a yield of 81.6 percent and that methyl 2-hydroxypropanoate was produced in a yield of 4 percent, based on the vinyl acetate reactant charged. Note that each of the products is hydrolyzable to lactic acid.

EXAMPLE 2

0.50 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Thirteen mole percent, based on vinyl acetate, of a catalyst comprising  $Pd(P\phi_3)_4$  plus 10 mole percent HCl were added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 77 percent

and that methyl 2-hydroxypropanoate was produced in a yield of 4 percent, based on the vinyl acetate reactant charged. Note that each of the products is hydrolyzable to lactic acid. Conversion of vinyl acetate was 89.2 percent.

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EXAMPLE 3

0.50 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Ten mole percent, based on vinyl acetate, of a catalyst comprising  $\text{RhCl}_3 \cdot \text{H}_2\text{O}$  plus 10 mole percent of HI was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 40 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that 2- acetyloxypropanoate was produced in a yield of 10 percent and that methyl 2-hydroxypropanoate was produced in a yield of 5 percent, based on the vinyl acetate reactant charged. Note that each of the products is hydrolyzable to lactic acid.

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EXAMPLE 4

0.50 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Ten mole percent, based on vinyl acetate, of a catalyst comprising  $\text{NiI}_2 \cdot 6\text{H}_2\text{O}$  was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 40 hours with

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stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 4.8 percent, based on the vinyl acetate reactant charged.

#### EXAMPLE 5

0.50 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Ten mole percent, based on vinyl acetate, of a catalyst comprising  $(\phi_3P)_2Ni(CO)_2$  was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44.25 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 4.6 percent, based on the vinyl acetate reactant charged.

#### EXAMPLE 6

0.50 mmoles vinyl acetate and 25.0 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Ten mole percent, based on vinyl acetate, of a catalyst comprising  $Pd(P\phi_3)_4$  plus 10 mole percent HCl co-catalyst was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with stirring. At the termination of the reaction, it was found that the

conversion of vinyl acetate was 100 percent. The reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 69.5 percent and that methyl 2-hydroxypropanoate was produced in a yield of 24.4 percent, based on the vinyl acetate reactant charged. Note that each of the products is hydrolyzable to lactic acid. The product solution was clear, with no precipitate evident.

#### EXAMPLE 7

5 mmoles vinyl acetate and 5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. One mole percent, based on vinyl acetate, of a catalyst comprising  $[\text{Rh}(\text{CO})_2\text{Cl}]_2$  was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 48.25 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 0.14 percent, based on the vinyl acetate reactant charged.

#### EXAMPLE 8

0.50 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. Ten mole percent, based on vinyl acetate, of a catalyst comprising  $\text{Pd}(\text{OAc})_2$  was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb

was heated to 100°C and allowed to react for 40 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 6 percent based on the vinyl acetate reactant charged.

#### EXAMPLE 9

0.475 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. 2.2 mole percent, based on vinyl acetate, of a catalyst comprising bis(triphenylphosphine)dichloropalladium,  $(\phi_3P)_2PdCl_2$  plus 4.2 mole percent  $P\phi_3$  co-catalyst, was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 19.5 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 84.3 percent and that methyl 2-hydroxypropanoate was produced in a yield of 2.7 percent, based on the vinyl acetate reactant charged. Note that each of the products is hydrolyzable to lactic acid. Vinyl acetate conversion was 95.2%.

#### EXAMPLE 10

0.57 mmoles vinyl acetate and 5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. 8.7 mole percent, based on vinyl acetate, of a catalyst comprising bis(triphenylphosphine)dichloropalladium,  $(\phi_3P)_2PdCl_2$  was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction

mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 79.9 percent and that methyl 2-hydroxypropanoate was produced in a yield of 12.6 percent, based on the vinyl acetate reactant charged. Note that each of the products is hydrolyzable to lactic acid, so that the yield of products useful to make lactic acid was 92.5 percent. Conversion of vinyl acetate was 100 percent.

#### EXAMPLE 11

0.50 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. 10.9 mole percent, based on vinyl acetate, of a catalyst comprising  $\text{Pd}(\text{P}\phi_3)_4$ , was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 850 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 43.5 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 35.1 percent.

#### EXAMPLE 12

0.486 mmoles vinyl acetate and 2.5 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. 10.5 mole percent, based on vinyl acetate, of a catalyst comprising bis(triphenylphosphine)dichloropalladium,  $(\phi_3\text{P})_2\text{PdCl}_2$ , was added. 0.05 mmoles toluene was included

as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that methyl 2-acetyloxypropanoate was produced in a yield of 68.5 percent.

#### EXAMPLE 13

0.542 mmoles vinyl acetate and 2.74 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. 5.2mg. of  $P\phi_3$  was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that no methyl 2-acetyloxypropanoate or 2-hydroxypropanoate was produced.

#### EXAMPLE 14

0.548 mmoles vinyl acetate and 2.85 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. No catalyst was added. 0.05 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with



stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that no methyl 2-acetyloxypropanoate or methyl 2-hydroxypropanoate was produced.

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EXAMPLE 15

0.530 mmoles vinyl acetate and 2.70 mmoles methanol were charged into a 71 cc stainless steel bomb equipped with a glass liner and a Teflon coated stir bar. One mole percent, based on vinyl acetate of HCl was added. 0.05  
10 mmoles toluene was included as an internal standard. Five milliliters of tetrahydrofuran as a solvent were also included in the reaction system. The reaction mixture was charged under argon. The bomb was sealed and carbon  
15 monoxide at a pressure of 1000 psi (at room temperature) was charged to the bomb, and the bomb was heated to 100°C and allowed to react for 44 hours with stirring. At the termination of the reaction, the reaction products were analyzed by gas chromatography and it was found that no methyl 2-acetyloxypropanoate or methyl 2-hydroxypropanoate  
20 was produced.

EXAMPLE 16

1.2 grams of methyl 2-acetyloxypropanoate was hydrolyzed to lactic acid by adding it with stirring to 15mL of 2N aqueous HCl solution. The reaction mixture was  
25 stirred at reflux for 4 hours. The reaction mixture was cooled to room temperature, and CaCO<sub>3</sub> was added slowly and carefully in small portions with stirring until the product solution was neutral to pH paper. Water was removed at high vacuum, and the white solid product was shown by  
30 NMR spectroscopy to contain 0.74g of calcium lactate (84% yield).

EXAMPLE 17

35 
$$1.0 \text{ g } \text{CH}_3\overset{\text{OH}}{\underset{|}{\text{CH}}}\text{CO}_2\text{CH}_3 \text{ (9.6 } \mu\text{mol) was hydrolyzed to lactic acid by adding it with stirring to 20mL of 2N aqueous HCl}$$

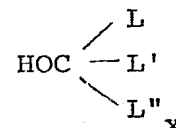
5 solution. The reaction mixture was stirred at reflux for 1 hour. The reaction mixture was cooled to room temperature and  $\text{CaCO}_3$  was added slowly and carefully in small portions with stirring until the product solution was neutral to pH paper. Water was removed at high vacuum, and the white solid product was shown by NMR spectroscopy to contain 1.03g of calcium lactate (98.3% yield).

10 As will be evident to those skilled in the art various modifications of this invention can be made or followed in the light of the foregoing disclosure and discussion without departing from the spirit and scope of the disclosure or from the scope of the claims.

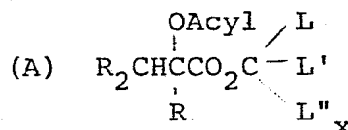
CLAIMS:

1. A process for producing a 2-hydroxy acid which comprises;

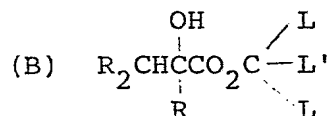
(1) intimately admixing and reacting an enol acylate  $R_2C=C(OAcyl)-R$  with CO and a hydroxyl compound



which is free of ethylenic or acetylenic unsaturation, to produce an acyloxy ester,

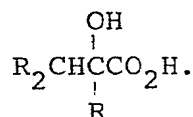


or a hydroxy ester



or both, wherein each R is H or C<sub>1</sub> to C<sub>30</sub> hydrocarbyl, usually H or C<sub>1</sub> to C<sub>10</sub> hydrocarbyl, and each R is the same or different, and L, L' and L'' are each H or an organic radical and L and L' can be members of a ring together with C, and X is either zero or 1 as necessary to satisfy the valence of the carbon atom, and wherein each of L, L', L'' and Acyl radicals can contain up to 30 carbon atoms, and wherein said enol acylate is free of acetylenic unsaturation and contains only one ethylenic double bond, and

(2) hydrolyzing the products of step (1), compounds (A) or (B), or both, to produce said 2-hydroxy acid,



2. A process of claim 1 wherein each of L, L', L'' and said acyl radicals can contain up to 10 carbon atoms and wherein each R group is limited to a maximum of 10 carbon atoms, all of which are members of an open chain hydrocarbyl group.

3. A process as claimed in claim 1 or claim 2 characterised in that each of L, L' and L'' and the

residue of the Acyl group attached to the Acyl O atom is hydrocarbyl.

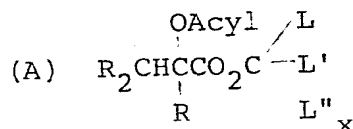
4. A process as claimed in any of claims 1 to 3 characterised for making lactic acid wherein each R is H.

5. A process as claimed in claim 1 or 4 characterised in that the hydroxyl compound reactant is C<sub>1</sub> to C<sub>4</sub> hydroxyalkane or phenol.

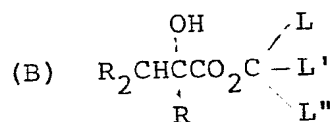
6. A process for making ester precursors of 2-hydroxy acids which comprises intimately admixing and reacting an enol acylate  $R_2C=C(OAcyl)R$  with CO and a

hydroxyl compound  $HOC(L)(L')(L'')_x$  which is free of ethylenic

or acetylenic unsaturation, to produce an acyloxy ester,



or a hydroxy ester



or both, wherein each R is H or C<sub>1</sub> to C<sub>30</sub> hydrocarbyl, usually H or C<sub>1</sub> to C<sub>10</sub> hydrocarbyl, and each R is the same or different, and L, L' and L'' are each H or an organic radical and L and L' can be members of ring together with L and L' and x is either zero or 1 as necessary to satisfy the valence of the carbon atom, and wherein each of L, L', L'' and said Acyl radicals can contain up to 30 carbon atoms, and wherein said enol acylate is free of ethylenic or acetylenic unsaturation and contains only one ethylenic double bond.

7. A process as claimed in claim 6 characterised in that L, L', L'' and said acyl radicals can contain up to 10 carbon atoms and wherein each R group is limited to a maximum of 10 carbon atoms, all of which are members of an open chain hydrocarbyl group.

8. A process as claimed in claim 6 or claim 7 characterised in that each of L, L' and L" and the residue of the Acyl group attached to the Acyl O atom is hydrocarbyl.

9. A process as claimed in claim 6 characterised for making lactic acid precursors wherein each R is H.

10. A process as claimed in claim 6 characterised in that the hydroxyl compound reactant is a C<sub>1</sub> to C<sub>4</sub> hydroxyalkane or phenol.

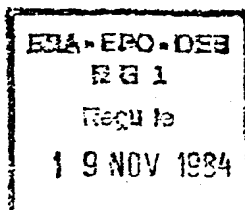
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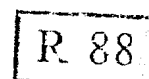
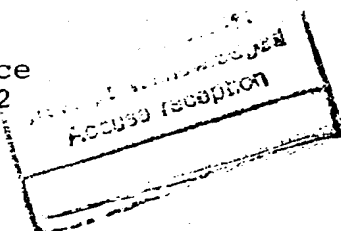
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8th November 1984

European Patent Office  
Directorate General 2  
Erhardtstrasse 27  
D-8000 Munchen 2  
GERMANY



Dear Sirs,

Re: European Patent Application 84305611.0  
The Standard Oil Company

We respectfully request that the following minor amendments may be allowed in the specification:

✓ Page 18, claim 1 formula (B) change "L" to read "L"x".

✓ Claim 1, line 5 after formula (B) change "X" to read "x".

✓ Page 19, formula (B) amend "L"" to read "L"x".

Substitute pages 18 and 19 are filed herewith in triplicate.  
No other changes have been made on these pages.

Yours faithfully,

SYDNEY SMITH

European Patent Attorney

Elkington and Fife

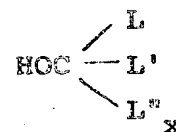
The request for correction is allowed under  
R. 88 EPC / with the exception of the deleted  
points /.

THE HAGUE,  
RECEIVING SECTION

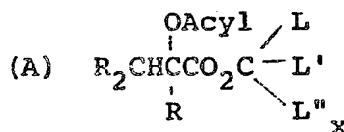
CLAIMS:

1. A process for producing a 2-hydroxy acid which comprises;

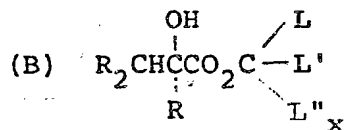
(1) intimately admixing and reacting an enol acylate  $R_2C=C-O-Acyl$  with CO and a hydroxyl compound



which is free of ethylenic or acetylenic unsaturation, to produce an acyloxy ester,

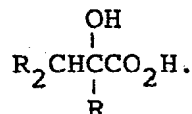


or a hydroxy ester



or both, wherein each R is H or C<sub>1</sub> to C<sub>30</sub> hydrocarbyl, usually H or C<sub>1</sub> to C<sub>10</sub> hydrocarbyl, and each R is the same or different, and L, L' and L'' are each H or an organic radical and L and L' can be members of a ring together with C, and x is either zero or 1 as necessary to satisfy the valence of the carbon atom, and wherein each of L, L', L'' and Acyl radicals can contain up to 30 carbon atoms, and wherein said enol acylate is free of acetylenic unsaturation and contains only one ethylenic double bond, and

(2) hydrolyzing the products of step (1), compounds (A) or (B), or both, to produce said 2-hydroxy acid,



2. A process of claim 1 wherein each of L, L', L'' and said acyl radicals can contain up to 10 carbon atoms and wherein each R group is limited to a maximum of 10 carbon atoms, all of which are members of an open chain hydrocarbyl group.

3. A process as claimed in claim 1 or claim 2 characterised in that each of L, L' and L'' and the

88

residue of the Acyl group attached to the Acyl O atom is hydrocarbyl.

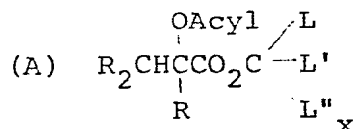
4. A process as claimed in any of claims 1 to 3 characterised for making lactic acid wherein each R is H.

5. A process as claimed in claim 1 or 4 characterised in that the hydroxyl compound reactant is C<sub>1</sub> to C<sub>4</sub> hydroxyalkane or phenol.

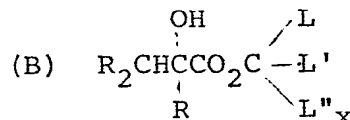
6. A process for making ester precursors of 2-hydroxy acids which comprises intimately admixing and reacting an enol acylate  $R_2C=C(OAcyl)R$  with CO and a

hydroxyl compound  $HOC(L)(L')(L'')_x$  which is free of ethylenic

or acetylenic unsaturation, to produce an acyloxy ester,



or a hydroxy ester



or both, wherein each R is H or C<sub>1</sub> to C<sub>30</sub> hydrocarbyl, usually H or C<sub>1</sub> to C<sub>10</sub> hydrocarbyl, and each R is the same or different, and L, L' and L'' are each H or an organic radical and L and L' can be members of ring together with L and L' and x is either zero or 1 as necessary to satisfy the valence of the carbon atom, and wherein each of L, L', L'' and said Acyl radicals can contain up to 30 carbon atoms, and wherein said enol acylate is free of ethylenic or acetylenic unsaturation and contains only one ethylenic double bond.

7. A process as claimed in claim 6 characterised in that L, L', L'' and said acyl radicals can contain up to 10 carbon atoms and wherein each R group is limited to a maximum of 10 carbon atoms, all of which are members of an open chain hydrocarbyl group.





European Patent  
Office

# EUROPEAN SEARCH REPORT

0144118

Application number

DOCUMENTS CONSIDERED TO BE RELEVANT			EP 84305611.0
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl. 4)
A	DE - A1 - 2 623 673 (MONSANTO CO.) * Claims * --	1,4,6, 9	C 07 C 69/68 C 07 C 59/08 C 07 C 67/38
A	DE - A1 - 3 210 617 (KURARAY CO., LTD.) * Claims * ----	1,4,6, 9	C 07 C 51/00
			TECHNICAL FIELDS SEARCHED (Int. Cl. 4)
			C 07 C 59/00 C 07 C 67/00 C 07 C 69/00
The present search report has been drawn up for all claims			
Place of search VIENNA		Date of completion of the search 28-11-1984	Examiner HOFBAUER
<b>CATEGORY OF CITED DOCUMENTS</b>			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	